Suspected hemophagocytosis in EBV infection

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Patient history

- 13-year-old girl, 1st pregnancy, prolonged labour, Caesarian section, short phototherapy
- Atopic eczema, no severe illness
- Full vaccination + hepatitis A, B
- Healthy unrelated parents
- No siblings

Patient history

- Febrile for 6 days (40 °C), 5th and 6th day non-reactive to antipyretics
- Sore throat, malaise, vomiting, cough
- CXR neg., CRP 18, ESR 10/25, leu 12, hb 120, tr 79, 49% atypical lympho in diff. count, myelo + metamyelocytes
- 6th day admitted to local pediatric department

Admission to local hospital

- 171 cm, 66 kg, febrile, icteric sclerae and skin, lymphadenopathy, pharyngitis, lacunar tonsilitis, liver +4 cm, palpable spleen, healed transverse cutting scars on left wrist
- Medication: clarithromycin 500 mg per day, paracetamol 1000 mg q nearly 4 hours

Local hospital stay – 7 days

- Leu 12…6, tr ~ 70, Hb 114…85
- Atypical lymphocytes, immature forms
- INR 1,2…1,9, ATIII 85%
- CRP max ~65, bili 46/38…98/88
- ALT 4-8, AST 9-11, GMT 4…11, LD ~50, ferritin ~1000, TAG 2,5
- IgG 13, IgA 2, IgM 2, IgE 1500
- Homogeneous hepatosplenomegaly, thickened gall bladder wall, multicystic expansion of right ovary
- Negative hepatitis investigation, positive EBV
- Mild bilateral fluidothorax
- Transferred to Dept. of Infectious diseases UH HK

Dept. of Infectious diseases UH HK
(3 days)

- Febrile, icteric
- Fluidothorax, ascites
- Elevated liver enzymes, ammonium ~ 150, chol 4.5, TAG 2.27, alb 26, leu 5…4,7, hb 85…76, tr ~70, FBG 1.29
- Infectious investigation
- Plasma for coagulopathy
- Corticosteroids for exanthema (toxoallergic ?)
- Transferred to Pediatric Department

Pediatric Department
overview at admission

- Acute hepatic failure, cholestasis
- Generalised lymphadenopathy
- Hepatosplenomegaly
- Maculo-papular rash
- Polyserositis
- Pancytopenia (leu 3,81)
- Expansion of right ovary
- Suicidal tendencies

Pediatric Department

- Differential diagnosis
  - viral (EBV…?) hepatic failure
  - toxic+viral hepatic failure
  - hemophagocytosis
  - infection
  - malignancy
  - autoimmunity
  - other (Wilson's disease, α1-AT deficiency, intoxication…)

Pediatric Department – autoimmunity ?

- All tested autoantibodies negative

Pediatric Department – malignancy ?

- Repeatedly normal tumor markers, no progression of ovarian pathology

Pediatric Department – other ?

- Normal copper, ceruloplasmin, α1-AT…

Pediatric Department – infection ?

- Positive PCR + „acute“ serology for EBV
- Negative PCR/serology for CMV, HIV, HCV, HPV B19, Listeria, Leptospira
- Positive HSV-IgM
- Threshold positive PCR Toxoplasma, KFR 1:512, ELISA – mildly increased IgM

Pediatric Department – HLH ?

- PB flow cytometry – roughly decreased number of B-lymphocytes (0.05/1,2%), elevated number of CD8 T-lymphocytes
- Bone marrow – dyserythropoiesis, monocytoid elements, no hemophagocytosis
- Exstirpation of inguinal lymph node – no hemophagocytosis
- Perforin positive

Pediatric Department – conclusion

- Severe course of EBV infection, possibly complicated by HSV, Toxoplasma, paracetamol + clarithromycin toxicity
  - acute hepatic failure
  - pancytopenia
- Regression of disease on corticosteroid, atb, supportive therapy

Follow-up

- Resolving fatigue, no severe illness, good antibody production

	12/2005	03/2006	06/2006	12/2006
EBNA IgM/IgG	-/+	±/-	+/+	+/+++
VCA IgM/IgG	0/±	-/+	-/+	0/+
EBV PCR	0	+	+	-
B-ly	0.05/1.5%	0.21/6.1%	0.19/3.9%	0.21/8.8%

Thank you for your attention !